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Immunoglobulin (Ig)-free light chains IgLC are present in serum and their production is augmented under pathological conditions such as multiple sclerosis, rheumatoid arthritis and neurological disorders. Until now, no (patho)physiological function has been ascribed to circulating Ig light chains. Here we show that IgLCs can confer mast cell dependent hypersensitivity in mice. Antigenic stimulation results in plasma extravasation, cutaneous swelling and mast-cell degranulation. We show that IgLCs have a crucial role in development of contact sensitivity, which could be completely prevented by a novel IgLC antagonist. Although IgE and IgG(1) are central to the induction of immediate hypersensitivity reactions, our results show that IgLCs have similar activity. IgLCs may therefore be a novel factor in the humoral immune response to antigen exposure. Our findings open new avenues in investigating the pathogenesis of autoimmune diseases and their treatments.

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